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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,159	05/03/2001	Yang-Dar Yuan	D2977	7424

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	21

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,159	YUAN ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *7-10,13-15 and 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 11, 12, 16, and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 2, 2003 has been entered.

Claims 1–26 are pending.

Claims 7-10, 13-15, and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Claims 1-6, 11, 12, 16, and 22-26 have been examined herein to the extent they read on the elected species, AGN 194310 (also known as 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid.

The outstanding rejection under 35 USC 103(a) is withdrawn in view of the amendments filed September 2, 2003 as the claims are drawn to the method of treating hyperlipidemia comprising administering an RAR antagonist without coadministering a retinoid to the mammal.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for RAR antagonists and inverse agonists disclosed in page 6 – 21 of the instant specification, does not reasonably provide enablement for other RAR antagonists and inverse agonists. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define neither a "RAR antagonist" nor an "RAR inverse agonists". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "RAR antagonist" and "RAR inverse agonists" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required because they are not structurally related and the instant specification fails to provide enough guidance and information for one of skilled in the art to ascertain these compounds. In other words, the instant specification merely describes functionally what compounds will do without disclosing what they really are. The instant claims read on all "RAR antagonist" or "RAR inverse agonists", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Please note that the compounds encompassed by the instant claims are more than the compounds disclosed in the instant specification. Without sufficient guidance provided in the instant specification, every compound known to men would be a potential candidate for the instant invention. One of skilled in the art would then be required to screen every known compounds in order to practice the full scope of the invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 1-6, 11, 12, 16, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation "without coadministering a retinoid to said mammal" recited in claims 1 and 25 is not supported by the originally filed specification or originally filed claims. The instant claims specifically exclude one specific agent in the method of treating hyperlipidemia. Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. [emphasis added] See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). See also MPEP 2163 and 2173.05(i).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 11, 12, 16, and 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klein et al. (US Patent 5,776,699) in view of Lenhard et al. (Biochemical Pharmacology, 2000;59:1063-1068) and Aberg et al. (Atherosclerosis, 1985; 54:89-97), Klein et al. and Aberg et al. are references of record in the previous office action mailed October 2, 2001.

Klein et al. teaches a group of RAR antagonists broadly, including the elected compound AGN 194310, being useful in inhibiting hypertriglyceride that are induced by the RAR receptor activation (See particularly Col. 3, line 45-col. 4, line 49; also col. 20, line 67).

Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid specifically in the method of lowering triglyceride. Klein et al. does not expressly teach the employment of 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to prevent myocardial infarction.

Lenhard et al. teaches HIV protease inhibitor Indinavir promoting dyslipidemia by increasing RAR signaling (See the abstract, also page 1067, col. 2). Lenhard et al. also teaches the employment of RAR antagonist 193109 can block the RAR signaling activation caused by indinavir (See the abstract).

Aberg et al. teaches that elevated serum triglyceride is one of the risk factor of developing myocardial infarction (See particularly page 89, third para.; also page 93, Table 1 and page 95, Table 3).

It would have been obvious to one skill in the art when the invention was made to employ AGN 194310 in a method to lower triglyceride level and prevent myocardial infarction.

One of ordinary skill in the art would have motivated to employ 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid in a method of lowering triglyceride level and preventing myocardial infarction because the RAR antagonists of Klein et al. are known to be useful in inhibiting hypertriglyceridemia caused by RAR activation. Therefore, employing any RAR antagonists of Klein et al., including 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid, would have been reasonably expected to be useful in a method of lowering triglyceride level that caused by RAR activation such as the administration of indinavir. Furthermore, it is known that elevated serum triglyceride increases the risk of developing myocardial infarction in patients. Therefore, patients taking 4-[[4-(4-ethylphenyl)-2,2-dimethyl-(2H)-thiochromen-6-yl]-ethynyl]-benzoic acid to lower their serum triglycerides level would be reasonably expected to prevent the development of myocardial infarction.

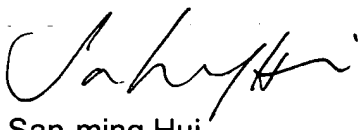
Response to Arguments

Applicant's arguments with respect to claims 1-6, 11, 12, 16, and 22-26 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



San-ming Hui
Patent Examiner
Art Unit 1617